American Journal of Pharmacy

AND THE SCIENCES
SUPPORTING PUBLIC HEALTH

PART OF THE ATKINS GARDEN IN
SOLEDAD-CIENFUEGOS, CUBA

(See Illustrated Article on Tropical Botany)

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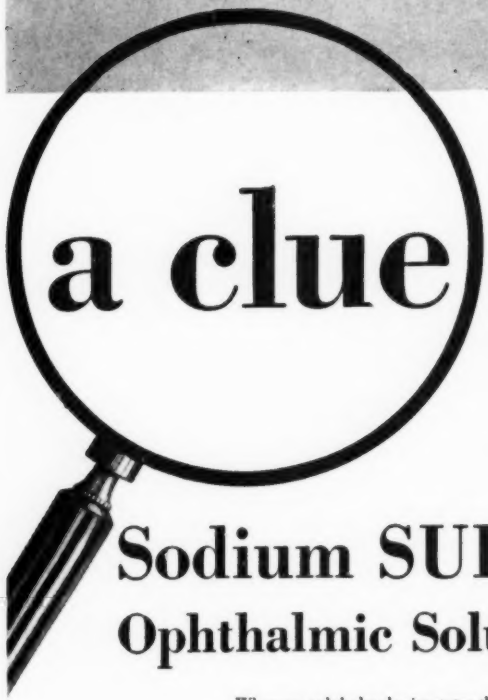

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EDITORIAL

THE PLANT WORLD

IN the earlier days of pharmacy one did not need to extol the virtues of plants and their value, for almost all important drugs were of plant origin. Even in relatively recent times the galenicals were of primary importance and pharmacognosy was given great stress in the pharmaceutical curriculum.

With the growth of synthetic organic chemistry great changes have taken place in the recognition given galenicals. Pharmacognosists are few in number and the course in pharmacognosy has been almost eliminated by some schools. Young teachers fresh from graduate school are chemistry-minded and they tend to scoff at the empiricism which is attached to the use of many galenical drugs. We, ourselves, feel somewhat more confident in the specificity of a pure organic compound as compared with the heterogeneous and variable mixture found in a vegetable drug. There is also much to be said for the advantages offered by a pure substance from the standpoints of uniformity of dosage, ease of control and the possibility of duplicating one's results. There can be no doubt but that the age of synthetics is here to stay for some time to come.

In our enthusiasm for developing new synthetics we, however, must not overlook the continuing importance of plants and plant products. It is somewhat trite to point out that without plants *all* animal life would cease. It is also a well known fact that most of the earth's storehouse of energy, the fossilized fuels, is of plant origin. When coal and oil reserves are depleted, as surely they must be someday, plant growth will become an even more important factor in our survival. By that time we may have learned how to capture the sun's energy—a feat accomplished by each cell of a green plant—but this the chemist still cannot do.

Careful reflection will bring to mind innumerable important drugs for which we are still dependent upon nature. No synthetic has yet approached digitoxin in its specific effect upon the myocardium. In many other instances a natural product has given us the clue concerning how to construct a molecule which would have specific therapeutic

applications. Quinine led to our modern antimalarials; tubocurarine, with its quaternary nitrogens, led to numerous muscle relaxants and even ganglionic blocking agents; and cocaine provided the clue for the large array of local anesthetics. Many other similar cases could be cited even including such drugs as chloromycetin.

Many old philosophers and even some of the clergy believed implicitly that God or nature provided somewhere in the plant kingdom a specific cure for each of the ills which afflict man. Some few still believe this theory and it would be just as hard to disprove it as to prove it. That there still exists innumerable valuable therapeutic aids, hidden somewhere in nature, seems a certainty. Finding them by systematic research is like looking for a needle in a haystack but someday probably by pure chance each will turn up.

Plants have, of course, a value to mankind other than their strictly practical uses. How drab our world would be without them! It seems as we grow older the beauty of nature means more and more to us. Flowers and trees which once were just a part of the passing scene now become things of exquisite beauty worthy of our rapt attention and stirring our inner emotions. Almost it seems that nature is preparing us for that inevitable and rapidly approaching time when we ourselves, insofar as our molecules and atoms are concerned, will again be blended into other living things about us. The nitrogen and carbon in the exquisite rose some years hence may once have been a part of those of us who live today. To love nature then is as understandable as to love ourselves for we are a part of it and will continue to be until the end of time.

L. F. Tice

A VISIT TO THE ATKINS GARDEN AND RESEARCH LABORATORY IN SOLEDAD-CIENFUEGOS, CUBA, IN JUNE 1951

By Theodor P. Haas, Ph. D.*

HARVARD University's tropical botanical garden, known as Atkins Garden and Research Laboratory, is situated in Soledad, near Cienfuegos, Cuba. The journey from Havana to Cienfuegos is through intensively cultivated sugar-cane fields, obviously planted recently. No forests are encountered, and husbandry is much in evidence. The dominant tree is the Royal Palm, *Roystonea regia* (H. B.) Cook, occasionally accompanied by very tall Kopak trees, *Ceiba pentandra*, L. with a whitish bark and large buttress roots.

Atkins Garden, on long lease from the Soledad sugar estate, covers an extensive area. Its headquarters is located at "Harvard House" (Plate #1) [1] where are found the laboratories, library and work rooms. In the garden a small house is reserved for work in germination, propagation, and for the planting of seedlings. A beautiful highway (Plate #2) leads from "Harvard House" to "Casa Catalina" on a hill top (Plate #3), and to the Garden itself. Casa Catalina is the guest house, where there are accommodations for eight students and four staff members. After the writer left Atkins Garden, this past July, the guest house was occupied by graduate students, who —under the leadership of a Harvard Professor—had the opportunity to become acquainted with tropical botany and its problems. Because

* Department of Biological Sciences, Philadelphia College of Pharmacy and Science.

[1] These pictures were made with a German camera "Kine Exakta." It is a single lens, mirror reflex camera (35 mm) which is extremely useful in the field and in the laboratory. As accessory tools the author uses a 20 cm long extension tube, and a f 5.5/180 mm telephoto lens "Tele-Megor." The former, which the author uses for close-up pictures, may be divided into different parts according to necessity. For this purpose the f 3.5 Zeiss Tessar lens may be removed from the camera and placed upon the extension tube. Two great advantages of the "Kine Exakta" are that one can see the picture on the screen before it is taken, and there are no difficulties with parallax. This enables the photographer to decide how large the close-up picture should be, and how many parts of the extension tube he needs. By using the entire tube and focusing the lens to 0.5 M. the latter can be placed as near as 6 cm from the object, and an enlargement of approximately 15 times may be obtained. The telephoto lens enables one to photograph landscapes, flowers, and inflorescences at a considerable distance. The illustrations in this article were taken with the "Kine Exakta." From the original kodachromes 35 mm black and white negatives were made and from these enlarged positives were developed.

the area of Soledad is relatively dry in August, the group moved to the Lancetilla Gardens near Tela, Honduras, which belongs to the United Fruit Company of Boston, and is situated in tropical rain forest. "Casa Catalina" is now the Director's residence, and preparations are being made to accommodate guests in "Harvard House", which is undergoing extensive alterations to provide more efficient working and living quarters. From "Casa Catalina" the visitor has a wonderful view of the far away Trinidad mountains (Plates #4 to 7).

Atkins Garden is mainly an arboretum, with trees and shrubs from the tropics of both hemispheres, palms included. There are also banana, sugar, cassava, and papaya plantations for experimental work. The administration of the garden is interested mainly in agronomy, that branch of agriculture dealing with field crops. From a list of the plants grown in the garden, the writer selected the names of those which were of pharmaceutical, economic, or purely botanical importance, and had a botanically trained native employee drive him with a "jeep" to the particular plants.

In the banana plantation fruit bananas are raised with fruits which can be eaten raw (Plate #8). Here are also found three specimens of *Musa textilis* Née, the pseudo-stem of which is very fibrous, and is used as "Manila hemp" for ropes because they do not weaken in ocean water nor rot so easily as do fibers from other plants. The fruits of *Musa textilis* are not edible, however, during the last war this plant was more important than the fruit banana, *Musa sapientum* L. *Musa textilis,* while native to the Philippines, is of South-Asiatic origin (Plate #9). The fruit banana, also of South-Asiatic origin, was brought to the Western hemisphere from West-Africa (it went with the slave trade across the whole of tropical Africa).

The banana is a tuber plant similar to the potato, but while the potato tuber lasts only one vegetation period, the banana tuber is persistent. It is rather big and has many dormant buds, like the potato. From these buds develop more or less tall pseudo-stems, formed by the enlarged petioles of the giant leaves. These enlarged petioles, the leaf sheaths, are arranged in a spiral. The whole structure is herbaceous and is easy to cut through it with a kitchen knife. The bananas are the largest herbs in the world. When the pseudo-stem has reached a certain age, the inflorescence pushes through on a long stalk. In the axils of big bracts are the banana flowers with their bent, inferior ovaries, arranged usually in two transversal rows. From

these banana flowers develop the seedless bananas which we eat. This can be seen very well on the Chinese dwarf banana, *Musa Cavendeshii* Lam. (Plates #10 and 11). The seeds are atrophied and no fertilization takes place; the fruits develop parthenocarpously. As with the potato, the propagation is done only asexually by planting the tuber or parts of it possessing buds.

There are two kinds of edible banana fruits, ones which can be eaten raw, and ones which can only be eaten fried (in fat) or baked. The latter is called plantain, and is abundantly eaten in Cuba. Botanically the banana fruit is a berry, the fleshy pulp of which contains a great amount of starch. In the banana which we eat raw this starch is converted largely into sugar during the ripening process. In contrast to this in the plantain the pulp remains starchy and does not taste sweet. Linnaeus named the fruit banana *Musa sapientum* and the plantain *Musa paradisiaca;* however, so great is the confusion today with respect to the nomenclature in the genus *Musa* that Kew Gardens is trying a re-classification.[2] Linnaeus saw bananas only in hot houses in Holland and today nobody knows what he actually saw.

A general view of the Atkins Garden is shown in Plate #12 with a tall Caryota palm in the foreground. In a rocky section of Atkins Garden are cultivated numerous, succulent Euphorbias (Plate #13). Native to tropical Africa, they live there under arid conditions like the cacti in the Western hemisphere, and are similar in their shape to the latter (the cactus shape is not limited to the cacti). Though some of the succulent Euphorbias still have leaves, their shoots are fleshy and green. The latter store water (therefore the plants are stem succulents), but contain chlorophyll and have the ability to assimilate, thus more or less replacing the leaves. Plate #14 shows a Cereus, a true cactus native to the Western hemisphere.

In illustration #15 we see the oldest part of Atkins Garden; here a dominant part is played by palms. Palms are the "Kings of the Tropics", and are not to be fully appreciated in our hot houses, where they are like birds in a cage. Palms must be seen outdoors; then it is easy to understand that botanists can become "palm crazy." Palms are differentiated according to their foliage: feather palms and fan palms. The Royal Palm, *Roystonea regia,* a feather palm, is the dominant tree in Western Cuba. Generally the large, old leaves with

[2] Kew Bulletin #2, 1948. "Classification of the Bananas" by E. E. Cheesman, Imperial College of Tropical Agriculture, Trinidad. "III Critical Notes on Species. *Musa paradisiaca* L., *Musa sapientum* L.

their large, green base drop off entirely from the trunk. The latter then appears a smooth greyish white, as if made of concrete. In other cases the bases of the leaves remain on the trunk. The vascular bundles of the leaves, containing silica, withstand decay longer than the rest of the tissue. For this reason the trunks of many palms, for example the Cabbage Palm, *Sabal* Sp. look more or less fuzzy. In some cases the fibers on the palm trunk are quite stiff and are used in the manufacture of brooms. Commercially these fibers are called "Piassava." The palms, belonging to the monocots, have no cambium circle, and therefore, wood in the botanical sense cannot be present. However, the tissue of the pith in which the vascular bundles are dispersed, may also contain silica, and may be extremely hard, as is the case with the stem of the coconut palm. The "wood" of this tree is called "porcupine wood" and is used for canes and furniture. The Royal Palm is economically very important, the trunk and leaves being used as building materials, and the oil-containing fruits are fed to pigs. The leaves provide a cool thatching for cottage roofs that lasts for as long as fifteen years.

The most spectacular impression was made upon the writer by an Asiatic fan palm, *Corypha umbraculifera* L, the Umbrella Palm (Plates 16, 17, 20, 21, 22, 23). In contrast to the Royal palm its trunk was densely covered with dead leaves, which were bent downward and remained on the trunk; only the upper part of the palm showed living large, green, fan leaves (Plate #20). As a rule, in all monocots, the stem can grow indefinitely, when the flowers or inflorescences are initiated laterally on the growing point, at which location in the bud, the formation of leaves and flowers as minute structures takes place. However, when flowers and inflorescences are initiated terminally fruiting exhausts the growing point, with the result that the plant or at least the flower producing shoot dies. For this reason the Agave dies after fruiting. As it can grow for many years before coming to bloom and fruit, the Agave is named "Century Plant". It takes, however, twenty not one hundred years to bloom. In contrast to this the Aloe which looks much like the Agave can grow indefinitely: and the inflorescences are lateral. Another interesting contrast of this type is found between the banana, the pseudo-stem of which dies soon after the ripening of the fruit; and the Traveler's Tree, belonging to the same family, which grows indefinitely because the inflorescences are lateral. In the case of the banana, one or several new pseudo-stems are produced from the tuber.

There is a similar situation with respect to palms. In most of them the inflorescences stay lateral, and can grow indefinitely in height; however, in the *Corypha* the inflorescence is situated terminally. Plates #18 and #19 show a flowering and fruiting Coconut Palm (photographed in Key West June 23, 1951). It was the writer's great fortune to see in the Atkins Garden a fruiting specimen of *Corypha umbraculifera* and he used all his photographic facilities (normal lens and telephoto lens), knowing that there are very few pictures in existence of this magnificent event. The author was told that this particular plant was twenty-two years old, and had started blooming in October 1950. As late as December 1951 it was still standing. Unfortunately, no photographs of the beginning of the flowering are available. In June 1951 the plant was fruiting; the lower leaves, still green, were bent downward above the dead leaves. The leaves, close to the infructescence took a horizontal position. The infructescence itself showed a pale yellow coloration, originating from still present flowers, but one could also see the very numerous globular, unripe, green fruits. The inflorescence—or infructescence axis, the direct continuation of the trunk of the palm, measured about a third of the latter. The whole palm, including the infructescence axis, was approximately 150 feet high (Plates #20 to 23). This was the situation in June in Soledad, but in tropical countries with more humidity the dead leaves rot much faster and drop off from the trunk. To complete the picture, a letter to the author from Dr. K. Biswas, Superintendent of the Indian Botanical Garden in Calcutta, dated September 6, 1951, may be quoted. Dr. Biswas writes: "Several species of Corypha grow in the Botanic Garden here and outside as well. They flower once in their lifetime after about 20-30 years according to the nature of the climate and the soil, and during the flowering period huge spathe burst with loud explosion and huge panicles come out giving magnificent view of the plant. Soon after the leaves fall off and by the time the fruits ripen, there is practically no leaf left. Huge quantities of seeds are produced and these seeds are used for manufacturing buttons."

Among the pharmaceutically important plants first may be mentioned *Cola acuminata* R. Br. native to Africa. The seeds of this plant contain caffeine and are used in making Cola beverages (Plates #25 and #26). The fruits are relatively large pods, staying together in variable numbers (sometimes 4, 3, 2 or 1). *Acacia Catechu* Willd was just blooming, with its small flowers and white filaments of the

stamens (Plate #26). Another legume which was in bloom was *Myroxylon toluifera* L., the plant from which tolu balsam comes. It showed little white flowers and young fruits. In these pod fruits only the terminal ovule develops to a seed. The other part of the pod, toward the peduncle, remains sterile and flat; in the ripe fruit it acts like a wing, similar to that of the maple fruit. During this visit *Haematoxylon campechianum* L. was not blooming, therefore, it was not possible to take pictures. However, the male plants of the nutmeg tree, *Myristica fragrans* Houtt. were in flower. The females were fruiting, but the fruits were smaller than usual, probably as a result of dry weather.

Flowering and fruiting at the same time was *Santalum album* L., the white sandal wood tree, probably a root hemiparasite. Of great importance as a perfume plant is *Cananga odorata,* (Lam.) Hook, f. & T. an Asiatic Anonaceae, from which Ylang-Ylang is obtained by enfleurage (Plate #24). The flowers have six lemon yellow petals, and exhale a marvelously delicate perfume. This plant is familiar throughout Havana, in many cases growing in back yards. The only pharmaceutically important plant which is also used as a display plant is the Golden Shower, cultivated in all tropics. Its scientific name is *Cassia fistula* L. and it is a legume. The long, woody pods, called Manna, contain a brown pulp which acts as a purgative. Such a tree was observed blooming in a private garden in Soledad. It had almost no leaves, but was full of bright yellow inflorescences (Plates #28 and #29). There are many beautiful display plants in the tropics: *Hibiscus* species with all varieties of flowers (our Rose of Sharon, *Hibiscus syriacus* L., does not grow in the tropics); *Quisqualis indica* L. with large white flowers which turn to red when they are old; *Bougainvillea spectabilis* Willd. with red or purple bracts surrounding the small cream-white flowers; *Poinciana regia* Boj.; the *Royal Poinciana;* the Flamboyant Tree from Madagascar; several *Plumeria* species; the *Frangipani* and many others. Plate #27 shows the cauliflory on the Jakfruit Tree, *Artocarpus heterophylla* Lam. with its huge, edible fruits appearing on the trunk. This plant is closely related to the Breadfruit tree and to the Osage Orange. In Plate #30 we see a Banyan, *Ficus bengalensis* L., with stem-like roots growing down from the branches.

Upon his return from the Atkins Garden the author visited the Botanical Garden and the Estation Experimental Agronomica in Santiago de las Vegas, a suburb of Havana. Here research work is

carried on with *Strophanthus* and *Dioscorea* species and on other medicinally important plants. The most interesting of these experiments is that concerned with *Hibiscus cannabinus* L., the Kenaf Plant, which is being carried on with the cooperation of the United States Department of Agriculture (Plates #31 and #32). The importance of this work can be understood if we consider the reasons behind it. The United States procures most of its sugar from Cuba; this sugar is shipped in jute bags, the materials for which come mainly from India and Pakistan. If we should be cut off from these countries, as happened during World War II with the rubber producing countries, our sugar import from Cuba would suffer. The jute plant, *Corchorus capsularis*, native to India and Pakistan, does not grow well in the Western hemisphere. A substitute, and a good one, for jute is Kenaf, *Hibiscus cannabinus* L.; which, despite the fact that it too is native to India and Pakistan, can be grown in the Western hemisphere. Therefore, by using Kenaf as a substitute for jute, enough material may be manufactured here to insure a sufficient number of containers for our sugar imports from Cuba.

One serious problem with respect to experiments with the Kenaf plant is that it is a "short-day" plant; one in which the length of the days influence the flowering of the plants. In herbaceous plants the stem stops growing in length, when the flowers begin to bloom. "Short-day" plants begin to bloom when the days are short (in contrast to this there are "long-day plants", which bloom when the days are long—flowering hormones may play a decisive part in this phenomenon though they have been isolated). In the tropics where Kenaf should be raised the days are relatively short; for example in June in Soledad the dawn starts approximately three quarters of an hour later than in Philadelphia, and twilight comes earlier also. During the author's stay, in June in Soledad twilight came between seven and seven-thirty P. M. Eastern Standard time. In moderate zones where the days are longer, the summer is rather short for Kenaf. We could raise tropical plants in Philadelphia because we have many aspects of tropical conditions—indeed many tropical weeds are found here—but for most tropical plants, which have a long vegetation period, the summer is too short. Another problem connected with this work is the need for machines to obtain the Kenaf fibers in an economical way. Experiments are being carried on currently to meet this need. The most promising source of these machines to date are Germany and France.

The Kenaf plants in the field differ from each other in the shape of their leaves, and some bloom while others do not. They do not follow the "short-day" pattern of the cultivated plants and do not have flowers. All old cultivated plants are hybrids of numerous varieties. When they are raised from seeds there is much segregation. If we were to raise our potatoes from seeds we would get plants with different qualities, from the plant with which we started, many of these qualities would be undesirable. Potatoes were hybridized by the American Indians who used them first. Fortunately we raise potatoes from the tubers which are not based on a sexual process, and which, therefore, have the same qualities as the mother plant. A similar situation is found in the date palm which was introduced to California.[3] The date palm is one of the oldest Old World cultivated plants, it was used by the Sumerians more than 5000 years ago. Herodotus tells us that only the off-shoots which the palm has at its base (Plate #33) are used for propagation. If the date palm were raised from seeds there would be produced dates with many different qualities. Beside this, being dioecious, approximately half of the plants would be male and produce pollen only.[4] The ancients knew that they had to pollinate the female flowers to prevent the dropping off of unfertilized fruit, and the fertilization of the date palm was a religious act. The Metropolitan Museum of Art in New York City has Assyrian stone reliefs from Assurbanipal's palace, showing a priest in the act of fertilizing the female date palm. Plate #34 shows a flowering male date palm.

Before the author left Cuba he paid a visit to a very unusual fan palm which he had seen small specimens of in the Atkins Garden. This palm is *Copernicia Torreana* León, a relative of the Brazilian wax palm *Copernicca cerifera* Mart. The wax of this palm is known as "Carnauba wax" and is used in the manufacture of record discs. *Copernicia Torreana*, native only to Cuba, has fan leaves without petioles, and its blades are attached directly to the trunk (Plate #35).

Upon his return to Miami the writer visited the Fairchild Tropical Garden; and Chapman Field, the experimental station of the United States Department of Agriculture. Here experiments are being carried on in an effort to obtain grafts of the *Chinese Sapin-*

[3] Bulletin #54, Bureau of Plant Industry, "Persian Gulf Dates and their introduction into America by David G. Fairchild, Agricultural Explorer, December 1903.

[4] Circular #728, U.S. Dept. of Agriculture, Washington D.C. "Date Culture in the United States," Roy W. Nixon, August 1945, revised March 1951.

daceae Litchi chinensis Sonn, the "Lytchee." The purpose of these experiments is to increase the number of tropical fruit trees cultivated in Miami; the fruits of which could then be sold to the big cities in the North as is done with mangos. The fruits of the trees in Chapman Field were just ripe during my visit, and tasted most delicious. Also cultivated here are bananas, cacao, date palms (both male and female) and many, many tropical plants.

At Chapman Field, experiments of vast importance are being carried on with *Hevea brasiliensis* Muell. the true rubber tree. This tree grows in the primeval forests of Brazil. In 1876 seeds were brought to Malaya, Java and other places in South Asia; and during the following years, the plantations there became the centers of the world production of natural rubber. During World War II the United States was cut off from this section of the world, and difficulties with the supply of natural rubber arose. Plants which were brought back from the Asiatic area to the Western hemisphere yielded more rubber than the native trees of Brazil, but were not resistant against fungus infections. In Chapman Field they are developing varieties which will have the rich yield of rubber of the plantation rubber trees and will be immune against the blight.

There is such a great difference between tropical plants growing outdoors and our poor hot house plants that one should try to see them in their native environment. The main reason that hot house plants are so different from out-door ones is that the glass of the green houses holds back most of the ultraviolet rays of the sunlight, and this inhibits the growth of the plants. Therefore, as Dr. David Fairchild said to this writer: "If you want to see tropical plants, you must go to the tropics."

The author is indebted to Dr. I. D. Clement, Director of "Atkins Garden and Research Laboratory" for checking this manuscript and giving useful suggestions.

DESCRIPTION OF PLATES.

PLATE 1. *Harvard House.* Here are the headquarters, laboratories, library, working rooms and also accommodations for guests.

PLATE 2. *Highway to "Casa Catalina."*

PLATE 3. *"Casa Catalina,"* formerly the guest house, now the Director's residence; it may now look somewhat different.

PLATE 4. *Highway to the Garden.* (The continuation of the highway, plate 2.)

PLATE 5. *View from "Casa Catalina"* to the Trinidad mountains. On the left side a part of the highway, shown in plate 4.

PLATE 6. do. (Taken with telephoto lens.)

PLATE 7. do. (In the foreground banana plantation.) (Taken with telephoto lens.)

PLATE 8. *Banana plantation.* There are young fruit banana plants (*Musa sapientum*).

PLATE 9. *Musa textilis,* fruiting.

PLATE 10. *Musa Cavendishii,* the Chinese dwarf banana. The whole plant, flowering. Chapman Field, Miami, Fla.

PLATE 11. do. Inflorescence, showing the big bracts, covering the banana flowers and dropping off later. Chapman Field.

PLATE 12. *General view of Atkins Garden* with a tall Caryota palm in the foreground.

PLATE 13. *Rock garden* with succulent Euphorbias (native to trop. Africa).

PLATE 14. *Cereus* (Cact[i]).

PLATE 15. *Oldest part of Atkins Garden.*

PLATE 16. *Corypha umbraculifera.* A non-blooming specimen and a blooming one in the background.

PLATE 17. do. inflorescence.

PLATE 18. *Cocos nucifera,* Cocos Palm, blooming and fruiting. The inflorescence stays lateral on the palm. The plant can grow indefinitely.

DESCRIPTION OF PLATES (Continued).

PLANT 19. do. inflorescence. The ball like structures are the female flowers; they become coco nuts. The rice grain-like structures are the male flowers. (Taken with the telephoto lens from the street in Key West.)

PLATE 20. *Corypha umbraculifera*, flowering. The inflorescence stays terminal. After fruiting, the plant will die.

PLATE 21. do. Inflorescence (Taken with the telephoto lens from the same spot).

PLATE 22. do. tip of the inflorescence (telephoto lens).

PLATE 23. do. base of the inflorescence (telephoto lens). The numerous fruits can be recognized.

PLATE 24. *Cananga odorata.*

PLATE 25. *Cola acuminata.* The plant is a shrub from Africa.

PLATE 26. do. fruits. From the caffeine-containing seeds, cola drinks are made.

PLATE 27. *Artocarpus heterophylla*, Jakfruit, The big fruits are edible. They appear on the trunk.

PLATE 28. *Cassia fistula, "Golden Shower."* The tree was covered with bright yellow flowers. Nearly no leaves were present. The legume fruits contain a pulp which is used as a purgative ("Manna").

PLATE 29. do. flowering branches.

PLATE 30. *Ficus bengalensis*, Banyan, with large, stemlike aerial roots.

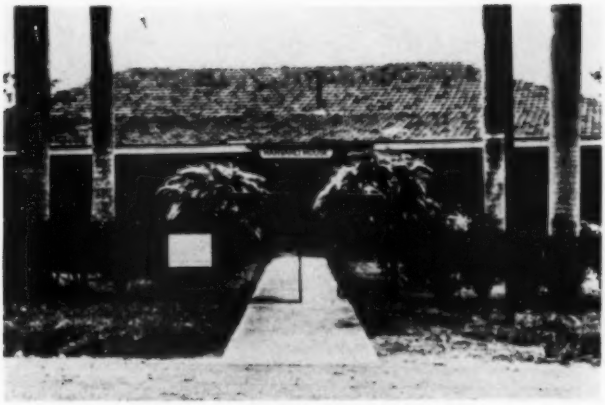
PLATE 31. *Hibiscus cannabinus*, Kenaf. The plants differ from each other by the form of their leaves. Some are blooming, others not. Photographed in Havana.

PLATE 32. do. Photographed in Havana.

PLATE 33. *Phoenix dactilifera*, female date palm. Infructescence (left) between the leaves. On the base (right) an offshoot. Chapman Field, Miami, Fla.

PLATE 34. Male date palm (species not identified). (Taken with the telephoto lens.) Chapman Field, Miami, Fla.

PLATE 35. *Copernicia torrcana.* The leaves without petioles. Photographed in Havana.



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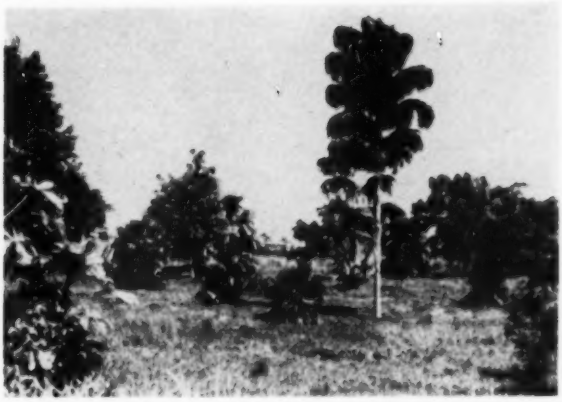

PLATE 12

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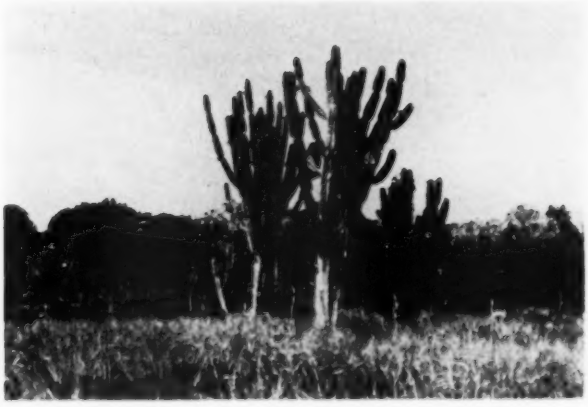

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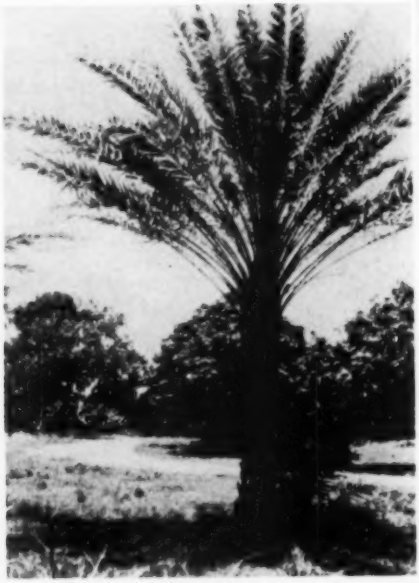

PLATE 33

PLATE 34

PLATE 35

MODERN APPROACHES TO ATHEROSCLEROSIS

A Review *

Cholesterol and the Phospholipids

ATHEROSCLEROSIS has been characterized as "the most important disease in America." (1) This is the type of arteriosclerosis which is overwhelmingly responsible for morbidity and mortality in man. (2)

Why do more Americans and Europeans die from atherosclerosis than Chinese or other rice-eating people of the Orient? Is diet responsible, or some other environmental factor? Or are death records merely more descriptive in the West than in the East. If the stress and strain of our modern life is to blame, why do ancient Egyptian mummies show evidence that their living counterparts died from the effects of atherosclerosis? Why do the arteries of young people develop degenerative changes, more appropriate to old age? Why do more men than women die from the heart trouble that results from the presence of atherosclerotic lesions?

These are among the questions that investigators are asking themselves. (3) Thus far the etiology and pathogenesis of atherosclerosis have eluded them. The problem is presently being attacked from a variety of angles, most of them involving lipid constituents of the blood. The following is a brief resume of the most prominent approaches with a definition of the basic chemical terms.

A. Lipid (which may be pronounced with short or long "i's" or any desired combination of the two) is a comprehensive term denoting all classes of fats.

B. The best-known lipid constituents (4) of the plasma are:

1) Neutral fat: Fatty acids (i.e. stearic, palmitic, etc.) esterified with glycerol

2) Free cholesterol (not esterified)

3) Cholesterol esterified with one or more of the fatty acids

* Based on articles appearing in *Calco Applications* (March and May 1952).

4) Phospholipids: Lecithins composed of glycerol esterified with two molecules of fatty acid and combined with phosphoric acid and a molecule of the nitrogenous base, choline. (Cephalins and sphingomyelins are other phospholipids containing different nitrogenous bases.)

All investigators agree that atherosclerosis involves a disorder in lipid metabolism. This conclusion has a reasonable basis in circumstantial evidence. In the first place, it has been demonstrated by morphologic examination that there is an excess of fat at the site of the lesions. Then too, atherosclerotic patients are known to have abnormally high blood lipid levels. Moreover, atherosclerosis can be produced in animals by deliberate interference with their metabolism of fat.

It was almost a half-century ago that cholesterol first became associated in the minds of investigators with atherosclerosis. (2) Experiments showed that it could be produced in rabbits by feeding them cholesterol. Many patients with atherosclerosis were found to have high blood cholesterol levels. The incidence of atherosclerosis is higher in overnourished people, who subsist on diets rich in natural sources of cholesterol. But the puzzling part of this situation is that there are atherosclerotic patients who have cholesterol levels within the normal range. It should be noted in this connection that normal values vary considerably. Fulton (4) states that they range from 123 to 274 mg. per 100 cc.

Normal phospholipid levels vary from 6.4 to 12.0 mg. per 100 cc. (4) Recently it was thought that the ratio of cholesterol to phospholipid might prove a more significant indication of atherosclerosis than the level of cholesterol alone. But while there is some evidence of correlation, here again clinical experience indicates that this ratio is probably just another variable in the disease.

At any rate the ultimate aim is not so much to be able to predict the people who will develop atherosclerosis as it is to find a means of diagnosis and a drug that will effectively prevent the condition or combat it once it appears. Since it is generally believed that the phospholipids are important to the metabolic transport of fat, the substances which make up such molecules might prove likely therapeutic agents. Unequivocal clinical evidence for the value of choline and other lipotropic substances in atherosclerosis has not yet appeared. While some clinicians (5) firmly believe that they are beneficial, others

say merely that their use is reasonable and not likely to prove harmful. (6)

Gofman's Contribution

The concepts just summarized have been the basis of much biochemical and clinical investigation in the field of atherosclerosis. Those concepts were concerned with the attempt to discover a cause-effect relationship between atherosclerosis and the dietary intake or the blood concentration of some specific lipid substance, such as cholesterol.

An entirely different approach currently appears very promising. There has long been evidence that a large proportion of the lipids of the serum occur not as small molecules, but as lipid aggregates, or lipoproteins, of varying complexity. (7) The new approach postulates that the physical state and particle size of the plasma lipids, rather than their concentration, is the clue to the etiology of atherosclerosis. (8, 9) In this field, the recent work of Gofman and his associates of the University of California at Berkeley has attracted a great deal of attention. Their own recent summary of their work deserves careful study. (10)

Gofman's experimental technique employs the ultracentrifuge as a means of separating the lipid constituents of human blood plasma to a sufficient degree to permit their classification. The following simple example illustrates the principle involved. Milk consists of a dispersion of particles of fat in an aqueous medium. The fat globules are of lower density than the aqueous medium and therefore tend to rise to the surface. In the increased gravitational field within a whirling centrifuge, the difference in densities is exaggerated, and the flotation rate of the fat globules—that is, their rate of travel in an "upward" direction—is increased.

Similarly, blood plasma contains a variety of lipoproteins—molecules containing protein, cholesterol, phospholipid, and neutral fat, in varying proportions. The lipoprotein particles studied by Gofman thus far vary widely in density, but all have a lower density than the plasma medium. In the ultracentrifuge, which develops a much more powerful gravitational force than the ordinary centrifuge, the lipoprotein particles tend to move in a direction opposite to that of the gravitational force, and the observed rate of travel of each particle depends upon the density of the particle. Thus the lipoproteins in a given sample of plasma may be separated and classified according to density.

Gofman uses the Svedberg, symbolized S_f, as a unit of classification. This is merely a unit of velocity, or rate of travel, under a given set of conditions, and is therefore a measure of the density of the lipoprotein. From Gofman's studies based on this principle has emerged the general picture that patients (and normals) show tremendous variations in the types and concentrations of lipoproteins present, but for a given individual at a steady state (i.e. not being acutely manipulated by diet, drug, or disease) there is a characteristic pattern of lipoproteins, stable over long periods, at least for portions of the lipoprotein spectrum.

Gofman and his group have been quite successful in establishing an association between certain classes of these lipoprotein molecules in the blood plasma, and clinical atherosclerosis. They showed that by measuring the plasma concentration of one class of the lipoproteins, designated S_f 12 to S_f 20, it was possible to segregate normal men from those with myocardial infarction much more accurately than on the basis of total serum cholesterol. The normal subjects had distinctly lower plasma concentrations of these particular lipoproteins than the patients, but using total serum cholesterol as the criterion the difference between the two groups was not nearly so clear-cut. Furthermore, the concentration of S_f 12-20 was considerably higher in male patients 20 to 40 years old than in female patients of the same age, a fact in accord with the lower incidence of atherosclerosis in females of this age. Patients over 40 years old, both male and female, showed significantly increased concentration of S_f 12-20 class molecules and lessened comparative differences, again corresponding to the relative incidence of atherosclerosis.

These workers have presented evidence that recurrence of myocardial infarction is associated with elevated S_f 12-20 values, and that these values can be reduced by restricting the total dietary fat and cholesterol intake. Even during the acute phase of myocardial infarction, the S_f 12-20 values appeared to be of prognostic significance. Out of 49 patients studied during the acute phase, 26 died and 23 survived. Of the 23 who survived, 17 had S_f 12-20 values below 60, while of the 26 who died, 20 had values above 60. Furthermore, of those 13 of the patients with values over 80, all died. The authors have found heparin to alter the lipoprotein spectrum in the direction of normality.

Already this series of studies have led to some systematization in the concept of the nature of blood lipid transport, and further far-reaching advances are to be expected. It is now quite clear that all

the major lipids in blood, including neutral fat, cholesterol, cholesterol esters and phospholipids, are transported in the form of giant lipoprotein molecules of several types. The various classes of these lipoproteins, represented by S_f values ranging from 4 to more than 40, appear to be uniform in that they all contain total cholesterol, phospholipid, and protein in equal proportions. Where they differ is in the degree of esterification of the contained cholesterol, and in neutral fat content. At one end of the lipoprotein spectrum, S_f above 40, fat comprises more than 75 per cent of the lipoprotein. As might be expected, because of the low density of fat itself, these molecules have the lowest density. At the other extreme, the S_f 4 class—the densest in the group studied—fat is absent or very low. The picture suggested is that the entire range of molecules of steadily decreasing fat content represents a sequence in a metabolic chain involved in the ultimate utilization of fat.

The uniform occurrence of phospholipid in substantial concentration in all these lipoproteins is in agreement with the work of other authors who have shown that phospholipids—compounds of fat, phosphoryl residues, and choline—are intimately involved in fat transport.

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SELECTED ABSTRACTS

The Iron Deficiency Anemia of Pregnancy. Lund, S. J., *Am. J. Obst. Gynecol. 62*:947 (1951). Determinations of plasma volume and erythrocyte protoporphyrin were used to augment routine hematological techniques in a controlled study of 66 normal and anemia pregnant patients. A high incidence of iron deficiency anemia was found among the 4,015 clinic patients screened by the author, on the basis of a minimum of 11 Gm. per cent hemoglobin for a normal pregnancy. However, only 66 patients returned a sufficient number of times to be studied.

Plasma volume increased, particularly in the last trimester during pregnancy, but the individual variations ranged from 14 to 121 per cent increase. This wide variation reduces the value of the red blood cell counts in an evaluation of the anemias of pregnancy. For, although the hemoglobin mass also increased in general, there was no correlation between the change in plasma volume and the change in hemoglobin mass.

A deficiency of iron causes an increase in the free erythrocyte protoporphyrin found in the blood cells. The erythrocyte protoporphyrin is the heme molecule deprived of its iron. A study of the levels of this substance aided in the detection of iron deficiency and also in the evaluation of treatment.

In this study 14 patients were used as normal controls and 10 patients were used as anemia controls. Seven normal patients received oral molybdenum ferrous sulfate throughout the last half of pregnancy and 39 anemia patients received therapy.

Only two patients failed to respond to the molybdenum ferrous sulfate therapy, standardized at 0.39 Gm. 3 times a day. There was an average increase in total hemoglobin mass in treated controls of 23 per cent and an increase of 71 per cent in anemia patients treated before the 36th week of pregnancy and 59 per cent in those treated after the 36th week. The untreated anemia patients showed a decrease in total hemoglobin mass and 5 had to be treated because of the severity of the anemia. Only one patient in the series had to discontinue therapy because of gastro-intestinal distress. The author also stated that the results obtained with this oral therapy were identical with those obtained with the use of intravenous iron.

Treatment of Barbiturate Poisoning. Locket, S. and Angus, J. *The Lancet 262*:580 (1952). Poisoning by barbiturates was studied in 84 consecutive patients. However, 20 of the cases were fully conscious when observed, were given a gastric lavage of normal saline or tap water and sent home. The 64 remaining patients were admitted to the hospital. Some of the patients were comatose, some stuporose, and some were conscious. Two of the patients who were comatose did not survive.

The treatment employed was lavage with 2 pints of normal saline or tap water. The patients then received 500,000 units of penicillin intramuscularly every 6 hours until they had been conscious for 48 hours. Oxygen was administered continuously by means of a mask or double nasal catheter, preferably at a rate of 10 liters per minute. The oxygen therapy was continued until respiration was normal, cyanosis had permanently disappeared, and consciousness had been fully restored. The oxygen aids in the amelioration of pulmonary edema, which often precedes pulmonary infection and pyrexia. Most necropsy records in barbiturate poisoning indicate the presence of bronchopneumonia. Therefore, penicillin was administered routinely.

The authors pointed out that this simple treatment routine, when coupled with prompt sensible and capable nursing care, will result in a very high rate of recovery. They do not feel that there is a need for the use of analeptics or drastic methods of treatment.

The Administration of Fat Emulsions. Shafiroff, B. G. P., *Trans. New York Acad. Sci. 14*:80 (1951). The administration of fat emulsions to man, either intravenously or by clysis with hyaluronidase, has been studied in a growing number of patients and promises to become a safe and practical method for providing calories for patients unable to assimilate food by normal alimentary processes.

The emulsion particularly referred to by the author was that of a 10 per cent combined emulsion which, in addition to coconut oil, contained 5 per cent glucose and protein hydrolysate and was stabilized by about 2.4 per cent gelatin. The caloric value of one liter was 1,289 calories. The important preliminary purification and depyrogenation of the oil prior to emulsification was accomplished by unspecified filtration methods removing bacteria and other material of 0.2 micron or larger. The oil was then washed with water and benzene in a process designed to remove toxic polysaccharides and thus pyrogen. The oil was then autoclaved and emulsified with the

other ingredients using a homogenization process sufficient to reduce the particle size to less than 1 micron. The viscosity of the finished emulsion was that of a free flowing liquid. It had a pH of about 6.5.

The author felt that the fever reactions observed in some patients was not due to pyrogenic material in this emulsion. In 87 per cent of the patients the temperature elevations were less than 1.9 degrees. In only 4 per cent of 750 patients did the temperature elevation exceed 3 degrees. In every case, however, the fever lasted for less than 24 hours. Headache was observed in 2.5 per cent of the patients, chills in 2 per cent, vomiting in 1.5 per cent and dizziness in 1 per cent. No patient was found to be sensitive to coconut oil. A striking observation was that many subjects who reacted to the first infusion of the fat emulsion showed little or no reaction on subsequent infusions.

The author stated that combinations of concentrated solutions of glucose with amino-acids cannot attain the caloric potency of combined fat emulsions without threatening cardio-vascular complications. There is less loss of lipids by excretion in the urine with an oxidation of as much as 50 per cent of the fat within the first 24 hours.

The Effect of Hexachlorophene Soap on the Bacterial Flora of the Hands. Lawrie, P. and Jones, B. *Pharm. J. 168:*288 (1952). The effectiveness of hexachlorophene soap, containing 2 per cent hexachlorophene, in reducing the bacterial flora of the hands was studied by the authors. The method employed involved pressing a sterile agar plate, provided with a gauze circle with a tab to facilitate removal of the agar circle, to the palm of the hand for 15 seconds. The agar circle was then replaced in the petri dish and incubated for 24 hours after which the number of colonies was counted. The washing procedure was compared with the scrubbing procedure, each being standardized. The scrubbing procedure was intended to similate a 10 minute surgical scrub.

The study involved 20 subjects classified as to the type of work they performed into office workers, light workers and heavy workers. The latter class of workers were those handling soil and other heavily contaminated materials.

The hexachlorophene soap brought about a reduction in the average bacterial count in all groups. The reduction in count over that of controls was greatest for the light workers with a reduction of 69 per cent in washing tests and 61 per cent in scrubbing tests. Heavy workers showed a reduction after washing tests of 55 per cent and

after scrubbing of 15 per cent. Office workers showed an average reduction after washing tests of 23 per cent.

The differences among the working groups was interesting. The much more pronounced difference among light workers was particularly significant because they included nurses, food handlers, and medical and surgical staff members. The statistically insignificant difference between the results following washing tests and following scrubbing tests led the authors to conclude that a thorough washing is as effective as a 10-minute scrub.

The authors pointed out that the test method did not give an absolute measure of the number of organisms on the skin, but they felt that it did give a measure of the number of organisms apt to be removed from the skin by handling surgical and other types of instruments.

A New Long-Acting Androgen, Testosterone Cyclopentylpropionate. Ott, A. C., Kuizenga, M. H., Lyster, S. C. and Johnson, B. A. *J. Clin. Endocrinol. Metabol. 12*:15 (1952). The duration of androgenic potency and the degree of response for the new androgen, testosterone cyclopentylpropionate, was compared with that obtained with free testosterone and testosterone propionate. The tests were conducted on young intact and castrated male rats by the subcutaneous injection of 5 mg. of each compound.

Testosterone cyclopenthylpropionate (TCP) was found to be still effective on the 30th day following injection in immature intact male rats. The duration and response of the seminal vesicle and prostate effect with TCP was greater than with free testosterone or testosterone propionate. By the 12th day the response to TCP was already triple that of an equal dose of the propionate. By the 30th day the increase was tenfold. Only when the dose of the propionate was increased to 25 mg. did the duration and response become comparable to TCP. Even then TCP showed a greater response on the 24th and 30th days.

It was found that a single injection of TCP was able to stimulate seminal vesicle and prostate growth so that by the 18th day it was practically equal to the growth expected from the animal's own testicular secretion. The authors pointed out that this was quite remarkable since the results of castration were given 4 weeks to become manifest. The weight of the accessory organs at the time of injection was 10 mg. as compared with 500 mg. for uncastrated controls.

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